Parenteral nutrition (PN) has changed the face of modern medicine, giving the chance of survival to millions of people around the world who, for various medical reasons, cannot nourish themselves via the gastrointestinal tract. While PN is a life-saving procedure, it is not free from disadvantages. It can cause both septic and metabolic complications. The most serious adverse effects of PN include PN-associated liver disease (PNALD), which is the result of long-term intravenous administration of a lipid emulsion and translocation of gut bacteria. It is estimated that up to 85% of home-depended PN patients develop PNALD.

PN is an intravenous supply of necessary nutrients, but its qualitative composition does not fully reflect all substances that are absorbed from the gastrointestinal tract under the conditions of standard oral nutrition. Patients receiving PN are deprived of the health benefits of natural bioactive compounds (NBCs) such as polyphenols, flavonoids, and anthocyanins, which are present in large amounts in vegetables and fruits.

Clinical studies on the search for therapeutic and preventive solutions in PNALD focus mainly on the elimination of soybean oil-based lipid emulsions rich in phytosterols from the PN admixture. Phytosterols are farnesoid X receptor (FXR) antagonists. This receptor is responsible for the regulation of the conversion of cholesterol to bile acids, and its inhibition by the compounds contained in PN is one of the main causes of cholestasis in the course of PNALD. Unfortunately, the consequence of replacing soybean oil-based lipid emulsions with animal oil-based emulsions may cause a deficiency of essential fatty acids, which is particularly undesirable in infants and children due to possible impairment of brain growth and development. Therefore, the search for an alternative method of PNALD treatment and prevention seems justified.

The aim of this project is to determine the role of selected natural FXR agonists (NFAs) in the prophylaxis and treatment of PNALD and to develop an intravenous pharmaceutical formulation enabling these compounds to be administered to parenterally fed patients.

During the project implementation, *in silico* and *in vitro* screening tests will be carried out, allowing the selection of NFAs from selected NBCs with proven hepatoprotective properties (honokiol, magnolol, withaferin, boswellic acid, nobiletin, tangerine, isorhamnetin, fisetin, cyanidin, delphinidin, malvidin, pelargonidin, peonidin, peonidinidin, petunidin) Then, studies on a cellular model will be carried out and an appropriate pharmaceutical formulation will be developed. In order to obtain the preparation with the best physicochemical properties, the Quality by Design concept will be applied. In the last stage, the developed pharmaceutical formulations with the most promising NFAs will be administered to animals in order to confirm the validity of the concept assumed in the project.

The proposed project aims to increase the safety of PN and reduce the incidence of complications related to nutritional therapy. The implementation of such tasks is in line with the current recommendations of international scientific societies dealing with PN issues. Undertaking pioneering research into the possibility of adding NFAs to PN admixtures and administering them to patients may revolutionize modern nutritional therapy.